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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,280	01/24/2005	Michael J Caulfield	20930P	8769

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
06/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,280	CAULFIELD ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *3,4,21,22,24 and 27-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-20,23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-63 are currently pending.

Election/Restrictions

Applicant's election of Group I, claims 1-30, and the species "bacteria," "phagocyte," and "*Streptococcus pneumoniae*" in the reply filed on 4/2/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 31-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 3, 4, 21, 22, 24, and 27-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/2/07.

Examination on the merits will commence on claims 1, 2, 5-20, 23, 25, and 26 ONLY, to the extent they read on the elected species where applicable.

Specification

The disclosure is objected to because of the following informalities: It recites numerous trademarks without providing adequate generic description thereof. Appropriate correction is required. The use of the trademarks "MILLIPORE MULTISCREEN" (page 4, lines 16-17, *inter alia*), "ELISPOT" (page 6, line 27), "DURAPORE" (page 7, line 25), "ZIPLOC" (page 9, line 7, *inter alia*), and

"IMMUNOSPOT" (page 9, line 28), among others, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The abstract of the disclosure is objected to because it contains phrases that can be implied ("A novel method is provided"). Correction is required. See MPEP § 608.01(b).

Claim Objections

The claims are objected to because the lines are crowded too closely together, making reading difficult. Future claim listings should comprise lines one and one-half or, preferably, double spaced. See 37 CFR 1.52(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9, 12, 13, 15, 18, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The method of claim 8 requires a "MILLIPORE 96 well HV plate," while that of claim 9 requires a "MILLIPORE MULTISCREEN HV 0.45μm Opaque Sterile Filtration

plate," both of which are trade names for particular products. Claim 15 requires the use of an "IMMUNOSPOT Analyzer," which is also a trade name. M.P.E.P. § 2173.05(u) recites, "It is important to recognize that a trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus a trademark or trade name does not identify or describe the goods associated with the trademark or trade name." If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. § 112, second paragraph. *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claims do not particularly point out the nature of the plates employed in the methods of claims 8 and 9 or the analyzer employed in the method of claim 15. Clarification is required.

Claim 18 recites "complement or active components thereof," but the claim does not set forth a particular activity for the active components. Clarification is required.

Claims 12, 13, and 19 recite components that are "capable of" various activities, but the claims do not require that these activities take place within the method. For example, claim 12 does not require that the device actually acquire any images, only that it have the ability to do so. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5-10, 12-15, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minnich et al. (2002, U.S. Patent 6,365,368; on 5/19/05 IDS) taken in view of Lehmann et al. (2002, U.S. Patent 6,410,252; reference A).

Minnich teaches a method for counting *E. coli* colonies comprising transferring liquid cultures containing various numbers of microbes to the wells of a 96-well nitrocellulose filter plate (column 6, lines 37-47); removing the culture media using suction filtration through the nitrocellulose filter, thus immobilizing the microbes on the filter (column 6, lines 49-51); adding a nonselective medium to each well and allowing the microbes to grow for 12 hours (column 6, lines 52-56); and assaying the presence of microbes using antibodies specific to said microbes (column 6, lines 58-67).

Minnich does not teach counting colonies of microbes on the filter plate. Minnich does not teach culturing the microbes on the filter plate for the time required in claim 7. Minnich does not teach a method for counting *S. pneumoniae* as required in claim 26.

Lehmann teaches a method of detecting, categorizing, and counting spots on a membrane comprising treating each filter (membrane) in a multiwell filter plate such that spots develop; capturing an image of each well in the plate; digitizing the images; and thresholding said images such that spots are detected, categorized, and counted (column 4, lines 40-54). Lehmann teaches that the step of treating the filter such that spots develop may comprise adding living cells to the well (column 3, lines 23-37). The plate of Lehmann is preferably a 96-well plate with a membrane at the bottom of each well (column 7, lines 50-53; Figure 1). While the working examples of Lehmann are drawn to monitoring T cell responses, Lehmann contemplates that the method may be used to assay suspensions of other biological materials (column 8, lines 10-12).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the spot counting step of Lehmann for the immunological detection step of Minnich because Minnich's method is a method for determining whether water has microbe contamination, so counting and identifying colonies of microbes within a sample is a functional equivalent for a positive result in an immunological assay designed to detect microbes. The skilled artisan would have further expected success in using the method of Lehmann to count bacterial colonies because Lehmann specifically teaches that the method may be used to enumerate spots of any kind, including suspensions of cells. The skilled artisan would have been motivated to substitute the counting step of Lehmann for the immunological assay of Minnich because the counting step does not necessarily destroy the cells, as the

immunological assay step does, so the contaminating microbes could be preserved for further study.

The person of ordinary skill in the art would have had a further reasonable expectation of success in using the method of Minnich in which the counting step of Lehmann has been substituted for the immunological assay step to enumerate *S. pneumoniae* because Lehmann teaches that the counting method has broad application to suspensions of all cells. The selection of type of bacteria to count using such a method would therefore have been a routine matter of optimization on the part of the artisan of ordinary skill. A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to assay for any bacteria using the method of Minnich in which the counting step of Lehmann has been substituted for the immunological assay step because the counting step and the immunological assay step provide similar information in terms of water contamination, and because the counting step may be applied to any cells.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Claims 1, 2, 5-10, 12-15, 25, and 26 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (2001, WO01/059157; on 5/19/05 IDS) taken in view of Lehmann et al. (2002, U.S. Patent 6,410,252).

Young teaches a method for enumerating bacterial colonies in a liquid sample comprising adding bacteria to a filter, incubating the bacteria from 1 to 24 hours such that colonies are formed, and counting the number of colonies on said filter (pages 2, 4, and 5). Young teaches removing excess media from the filter using a vacuum (page 2). The preferred filter of Young is one with hydrophilic regions separated from each other by hydrophobic partitions (page 4). Young teaches that any microorganism can be assayed using the method (page 2) and that any manner of enumerating the colonies may be used, so long as the colonies are counted (page 5).

Young does not teach a method in which colonies are assayed in a multi-well plate.

Lehmann teaches a method of detecting, categorizing, and counting spots on a membrane comprising treating each filter (membrane) in a multiwell filter plate such that spots develop; capturing an image of each well in the plate; digitizing the images; and thresholding said images such that spots are detected, categorized, and counted (column 4, lines 40-54). Lehmann teaches that the step of treating the filter such that spots develop may comprise adding living cells to the well (column 3, lines 23-37). The plate of Lehmann is preferably a 96-well plate with a membrane at the bottom of each well (column 7, lines 50-53; Figure 1). While the working examples of Lehmann are drawn to monitoring T cell responses, Lehmann contemplates that the method may be used to assay suspensions of other biological materials (column 8, lines 10-12).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the 96-well plate assay of Lehmann for the single filter assay of

Young because Young teaches that any membrane filter may be used in the method, so long as microorganisms can grow thereon (page 4). The skilled artisan would have been motivated to substitute the 96-well plate format of Lehmann for the single filter of Young for the expected benefit that many different samples could be evaluated in a single assay. Automating a manual activity (in this case, automating the manual examination of 96 single filters of Young by including them all in the single multiwell filter of Lehmann) is obvious. See M.P.E.P. § 2144.04.

The person of ordinary skill in the art would have had a further reasonable expectation of success in using the method of Young in which the multiwell format of Lehmann has been substituted for the immunological assay step to enumerate *S. pneumoniae* because Lehmann teaches that the counting method has broad application to suspensions of all cells and because Young teaches that any type of microorganism may be assayed using the method. The selection of type of bacteria to count using such a method would therefore have been a routine matter of optimization on the part of the artisan of ordinary skill. A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to assay for any bacteria using the method of Young in which the 96-well assay format of Lehmann has been substituted for the single filter assay because more samples could be evaluated in a single assay, and because the counting step may be applied to any cells.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over either either Minnich or Young taken in view of Lehmann as applied to claims 1, 2, 5-10, 12-15, 25, and 26, above, and further in view of Dodge et al. (2002, U.S. Patent Application Publication 2002/0051974; reference B).

The teachings of Young, Minnich and Lehmann are relied upon as above.

None of Young, Minnich, and Lehmann teaches removing excess media from the multiwell filter plate by centrifugation.

Dodge teaches that excess fluid may be removed from a 96-well filter plate by centrifuging the entire plate, thus allowing the fluid to pass through (paragraph 92).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the centrifugation step of Dodge for the vacuum filtration step of Minnich or Young because Dodge teaches that the centrifugation step removes excess fluid from the wells. The selection of the manner in which the media is removed from the wells in the method of Minnich or Young taken in view of Lenhmann would therefore have been a routine matter of optimization on the part of the artisan of ordinary skill. A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute the centrifugation step of Dodge for the

vacuum filtration step of Minnich or Young because the two steps are functional equivalents.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Claims 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Minnich or Young taken in view of Lehmann as applied to claims 1, 2, 5-10, 12-15, 25, and 26, above, and further in view of Fischer (1996, U.S. Patent 5,571,511; reference C).

The teachings of Young, Minnich and Lehmann are relied upon as above. In addition to these cited teachings, the method of Lehmann is explicitly taught as being useful for assaying the effects of growth factors and inhibitors, *e.g.*, on the cells being counted (column 10, lines 17-39). Furthermore, Minnich teaches including active agents in the wells with the bacteria (column 7, lines 32-54, *e.g.*) and Young teaches that multiple components may be added to the filter (page 3).

None of Young, Minnich, and Lehmann teaches adding an antimicrobial agent, an antiserum, complement, or engulfing cells such as phagocytes to the wells at any time, as required in claims 16-20.

Fischer teaches a method for assaying the effects of antibodies, serum, and neutrophils (which are phagocytes) on bacterial growth (Example 4, beginning at column 19, line 55). The opsonophagocytosis assay method of Fischer comprises adding washed neutrophils to the wells of 96-well microtiter plates along with growing

bacteria and rabbit serum that comprises antibodies against said bacteria (column 19, line 66, through column 20, line 4), then incubating the mixture and determining the number of bacterial colonies in each well. The serum of Fischer is a source of active complement (column 20, line 4) and is an "antimicrobial agent" in the respect that it kills at least some of the bacteria (Table II at column 20, lines 16-34).

A person of ordinary skill in the art would have had a reasonable expectation of success in adding a step to the method of Minnich or Young taken in view of Lehmann in which serum, complement, antibodies, an antimicrobial agent, or engulfing cells are placed into the well of the filter plate prior to the addition of bacteria and assaying the number of bacteria in the presence and absence of the added agent because Minnich, Young, and Lehmann all suggest assaying the effects of different active agents on cells in their methods (Minnich: column 7, lines 32-54; Young: page 4; Lehmann: column 10, lines 17-39). Furthermore, Fischer teaches that the opsonophagocytosis assay may be conducted in any format (column 14, line 60, through column 15, line 15). The skilled artisan would have been motivated to add an active agent or putative active agent to the wells in the method of Minnich or Young taken in view of Lehmann in order to determine the effects of said agent on the growth of bacteria, *e.g.* to determine whether a particular compound can reduce growth of a given species, and to identify the role of phagocytosis in the effectiveness of said agent.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the opsonophagocytosis assay of Fischer with the automated colony counting method of Minnich or Young taken in view of Lehmann

because Fischer teaches that the opsonophagocytosis assay may be conducted using any assay that provides a determination of opsonization potential, and because the method of Minnich or Young in view of Lehmann would provide such data *via* counting bacterial colonies in the presence and absence of active agent.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart